DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 20 2001

The Honorable Bart Stupak
House of Representatives
Washington, D.C. 20515-2201

Dear Mr. Stupak:

This is in follow-up to our meeting on December 6, and in response to your letter of May 25, 2001, addressed to Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration (FDA), regarding further studies on the prescription drug Accutane (isotretinoin). We apologize for the unacceptably long delay in responding to your letter, which was due to an inadvertent oversight.

As we discussed in our meeting with you on December 6, FDA's mission does not include the actual conduct of clinical research or comprehensive basic science research programs. We do understand your call for scientific study that is truly independent of the drug manufacturer. We remain hopeful that our efforts to increase awareness among the biomedical science community of central nervous system issues regarding Accutane will provide an impetus for obtaining independent data through the process of scientific discovery. However, we also understand the frustration inherent in the fact that scientific discovery is usually a slow incremental process.

As we noted in our discussion with you on FDA's Accutane Psychiatric Risk Management Program, we have pursued a number of avenues in an attempt to further the research on this drug.

- In 1997, FDA instructed Hoffman-LaRoche to investigate the association of Accutane and psychiatric adverse events. Numerous epidemiological studies have been completed and reviewed, but are inconclusive in FDA's opinion.
- FDA met with the National Institutes of Mental Health (NIMH) in early 2001 to solicit interest in clinical and basic

research on Accutane (isotretinoin). At this time, we are aware that the Molecular and Cellular Neuroscience Research Branch is involved in screening a series of retinoids, including isotretinoin, in laboratory tests for central nervous system activity. We are also planning a working meeting in the near future so that FDA and NIMH scientists can discuss technical issues in clinical study designs that FDA has been developing. We are not aware of any other current initiatives in this area at NIMH.

- CDER is currently preparing protocols and finalizing an interagency agreement with the Defense Department's Uniformed Services University of the Health Sciences to fund hypothesis-generating pre-clinical neuroscientific research.
- FDA has diligently pursued, with Hoffman-LaRoche, the development of a clinical trial protocol to address psychiatric effects of isotretinoin. Significant trial design problems remain to be solved before a trial that would yield meaningful data can be implemented.

Further, FDA is working aggressively to implement the recommendations of the Dermatologic and Opthalmic Drugs Advisory Committee held in September 2000.

Enclosed are copies of documents and publications that you requested on December 6, specifically:

1) *Journal of the American Academy of Dermatology*, November 2001;
2) *Newsletter of the Inflammatory Skin Disease Institute*, Fall 2001;
3) Supplement to *Skin and Allergy News*, Spring 2001;
4) Article: "Hypervitaminosis A Syndrome: A paradigm of retinoid side effects," *Journal of the American Academy of Dermatology*, May 1987;
5) Article: "Facts and Fiction about Teenagers and Acne," *Skin and Aging*, April 2001;
6) Bringing Acne Treatment to the Forefront, Supplement to *Dermatology Times*, November 2001
7) Article: "Isotretinoin link to depression unfounded," *Dermatology Times*, October 2001; and
8) Editorial: "Depressing News About Accutane," *Skin and Aging*, December 2000.

Thank you again for your continuing interest in this important matter. If you have additional questions, please let us know.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
for Legislation

Enclosures

cc: The Honorable James C. Greenwood
Chairman
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and Investigations
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